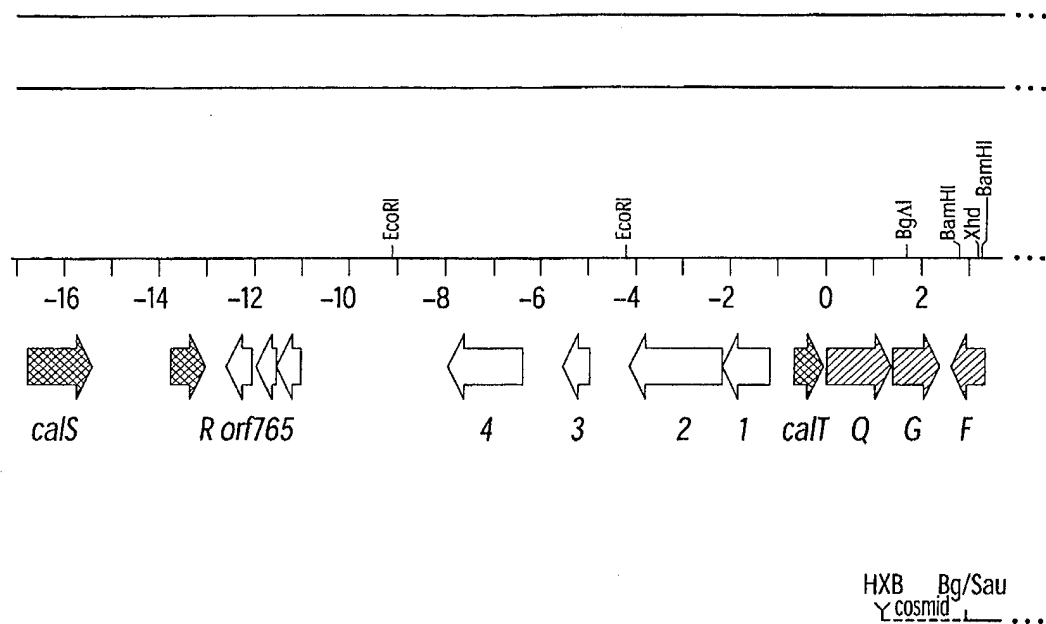


| Summary of cosmid clones isolated from <i>M. echinospora</i> genomic library. |                               |                                |                                |  |
|---|-------------------------------|--------------------------------|--------------------------------|--|
| clone <sup>a</sup>  | type I PKS genes <sup>b</sup> | type II PKS genes <sup>b</sup> | deoxy sugar genes <sup>b</sup> | resistance<br>( $\mu\text{g mL}^{-1}$ ) <sup>c</sup> |
| 3a  | N.D. <sup>d</sup>             | N.D. <sup>d</sup>              | N.D. <sup>d</sup>              | 0.5  |
| 4a  | N.D. <sup>d</sup>             | N.D. <sup>d</sup>              | N.D. <sup>d</sup>              | 0.5  |
| 4b  | +                             | +                              | +                              | 0.5  |
| 10a   | +                             | +                              | +                              | 0.5  |
| 13a   | +                             | +                              | +                              | 0.5  |
| 16a   | N.D. <sup>d</sup>             | N.D. <sup>d</sup>              | N.D. <sup>d</sup>              | 0.5  |
| 56  | +                             | +                              | +                              | 0.1  |
| 58  | -                             | -                              | +                              | < 0.01   |
| 60  | +                             | +                              | +                              | 0.05   |
| 66  | -                             | -                              | +                              | 0.04   |
| puc18/pBluescript <sup>e</sup>  | -                             | -                              | -                              | < 0.01   |

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FIG. 1



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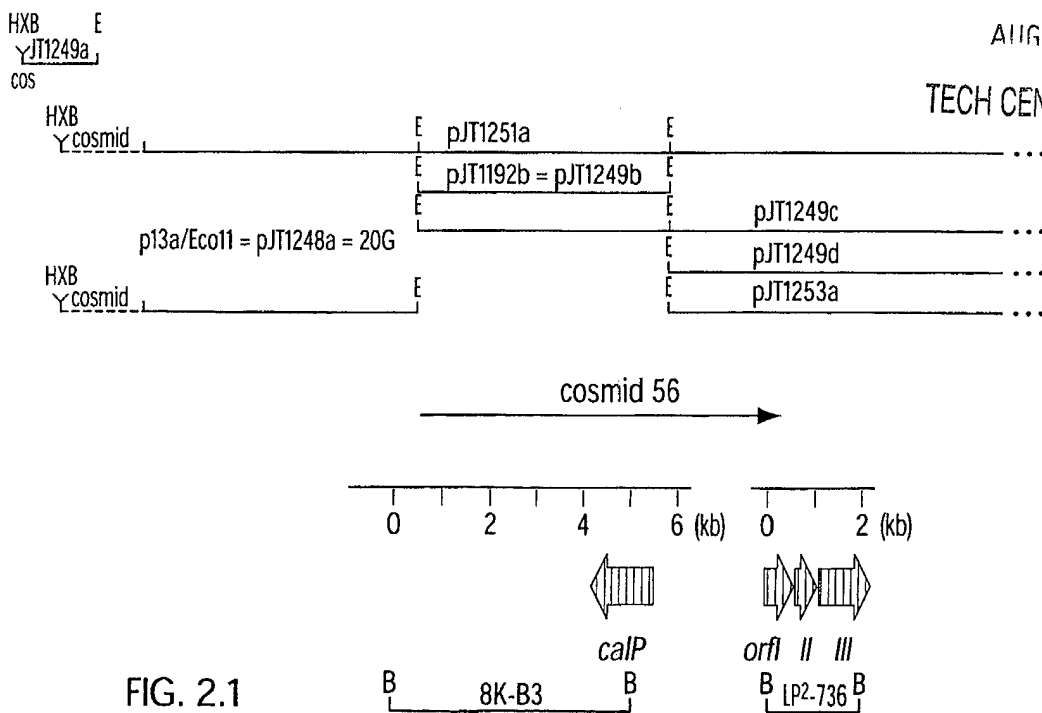


FIG. 2.1

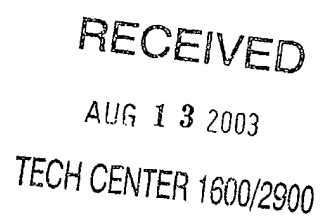
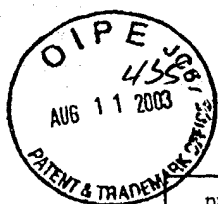


FIG. 2.2



| putative polypeptide | number of amino acids | proposed function or sequence similarity detected | probability            | start/stop codons | best match            |
|----------------------|-----------------------|---|------------------------|-------------------|-----------------------|
| CalA                 | 328                   | membrane transporter (ATP-binding)                | $5.4 \times 10^{-124}$ | ATG/TGA           | DrrA <sup>97</sup>    |
| CalB                 | 561                   | membrane transporter                              | $5.5 \times 10^{-70}$  | ATG/TGA           | DrrB <sup>97</sup>    |
| CalC                 | 181                   | calicheamicin resistance protein                  | confirmed              | ATG/TGA           |                       |
| CalD                 | 263                   | O-methyltransferase                               | $1.1 \times 10^{-99}$  | ATG/TGA           | AveBVII <sup>98</sup> |
| CalE                 | 420                   | glycosyltransferase                               | $4.7 \times 10^{-30}$  | GTG/TAG           | EryCII <sup>99</sup>  |
| CalF                 | 245                   | N,N-dimethyltransferase                           | $1.5 \times 10^{-78}$  | ATG/TGA           | DesVI <sup>100</sup>  |
| CalG                 | 990                   | TDP-D-glucose 4,6-dehydratase                     | confirmed              | GTG/TAG           |                       |
| CalH                 | 338                   | Perosamine synthetase                             | confirmed              | GTG/TGA           |                       |
| CalI                 | 568                   | Dipeptide transporter                             | $1.7 \times 10^{-24}$  | GTG/TGA           | DciAE                 |
| CalJ                 | 332                   | O-methyltransferase                               | $1.0 \times 10^{-37}$  | ATG/TGA           | DmpM                  |
| CalK                 | 440                   | L-cysteine/cystine C-S-lyase                      | $1.6 \times 10^{-28}$  | GTG/TGA           | C-DES                 |
| CalL                 | 562                   | Oligopeptide transporter protein                  | $9.5 \times 10^{-14}$  | ATG/TGA           | OppA                  |
| CalM                 | 416                   | Regulatory protein                                |                        | GTG/TGA           |                       |
| CalN                 | 398                   | Glycosyltransferase                               | $3.4 \times 10^{-79}$  | ATG/TGA           | Ole1                  |
| CalO                 | 331                   | Hexopyranosyl-2,3-reductase                       | $4.9 \times 10^{-139}$ | ATG/TGA           | EryBII                |
| CalP                 | (179)                 | Desaturase  | $5.7 \times 10^{-7}$   | /TGA              | CrtI                  |
| CalQ                 | 453                   | UDP-D-glucose 6-dehydrogenase                     | confirmed              | GTG/TGA           |                       |
| CalR                 | 282                   | Transcriptional regulator                         | $6.7 \times 10^{-11}$  | ATG/TGA           | SC5C7.03              |
| CalS                 | 1113                  | P <sub>450</sub> oxidase                          | $2.9 \times 10^{-66}$  | GTG/TGA           | BioI                  |
| CalT                 | 432                   | oxygenase/halogenase                              | $2.0 \times 10^{-62}$  | GTG/TAA           | PCZA361.20            |
| CalU                 | 377                   | glycosyltransferase                               | $2.0 \times 10^{-53}$  | ATG/TGA           | SnogE/D               |
| CalV                 | 125                   | $\beta$ -keto-acyl synthase III                   | $2.0 \times 10^{-65}$  | ATG/TGA           | SC4A9                 |
| CalW                 | (449)                 | cytochrome P450                                   | $1.0 \times 10^{-91}$  | GTG/TGA           | CYP105B1              |
| CalX                 | (197)                 | TDP-4-keto-6-deoxy-L-hexose 2,3-dehydratase       | $1.0 \times 10^{-22}$  | /TGA              | MtmV                  |
| 6MSAS                | (198)                 | orsellenic acid synthase                          | $6.5 \times 10^{-76}$  | ATG/              | AviM                  |
| ActI                 | (207)                 | polyketide cyclase                                | $3.0 \times 10^{-66}$  | /TGA              | CurF                  |
| ActII                | 136                   | polyketide cyclase                                | $5.0 \times 10^{-53}$  | ATG/TGA           | SchB                  |
| ActIII               | (308)                 | polyketide synthase                               | $8.6 \times 10^{-148}$ | GTG/              | Pms1                  |
| orf1                 | 322                   | unknown   |                        | ATG/TGA           |                       |
| orf2                 | 654                   | unknown   |                        | ATG/TGA           |                       |
| orf3                 | 373                   | integrase   | $3.0 \times 10^{-13}$  | ATG/TGA           |                       |
| orf4                 | 521                   | chromosome partitioning protein                   | $3.3 \times 10^{-10}$  | GTG/TAA           | ParA                  |
| orf5                 | 175                   | unknown   |                        | ATG/TGA           |                       |
| orf6                 | 139                   | unknown   |                        | ATG/TGA           |                       |
| orf7                 | 187                   | unknown   |                        | GTG/TGA           |                       |
| orf8                 | 266                   | regulatory protein                                | $3.0 \times 10^{-66}$  | ATG/TGA           | KorSA                 |
| OrfI                 | 127                   | hydroxylase                                       | $1.5 \times 10^{-7}$   | ATG/TGA           | SC4C6.24c             |
| OrfII                | 248                   | unknown   |                        | GTG/TGA           |                       |
| OrfIII               | 298                   | hydroxylase                                       | $3.3 \times 10^{-90}$  | GTG/TGA           | SCA32                 |
| OrfIV                | 363                   | unknown   | $5.3 \times 10^{-43}$  | GTG/TGA           | SC9C7.25              |
| OrfV                 | 288                   | aminotransferase                                  | $2.9 \times 10^{-37}$  | GTG/TGA           | SCF55                 |
| OrfVI                | 1012                  | glu-ammonia-ligase adenyltransferase              | exact                  | GTG/TGA           | SCA32                 |
| OrfVII               | 236                   | Methyltransferase                                 | $8.0 \times 10^{-63}$  | GTG/TAG           | SCF43A.25c            |
| OrfVIII              | 441                   | Integral membrane protein                         | $8.9 \times 10^{-9}$   | GTG/TGA           | SCA32                 |
| OrfIX                | 478                   | Integral membrane protein                         | $1.1 \times 10^{-21}$  | ATG/TGA           | MLB268                |
| OrfX                 | 504                   | Membrane protein                                  | $5.5 \times 10^{-20}$  | GTG/TGA           | B1496.F1.14           |
| OrfXI                | 251                   | Immunity resistance protein                       | $1.1 \times 10^{-9}$   | ATG/TGA           | TFXG                  |
| IS-element           | 1209 bp               | insertional element                               | $5.7 \times 10^{-168}$ |                   | IS1136 <sup>111</sup> |

FIG. 3

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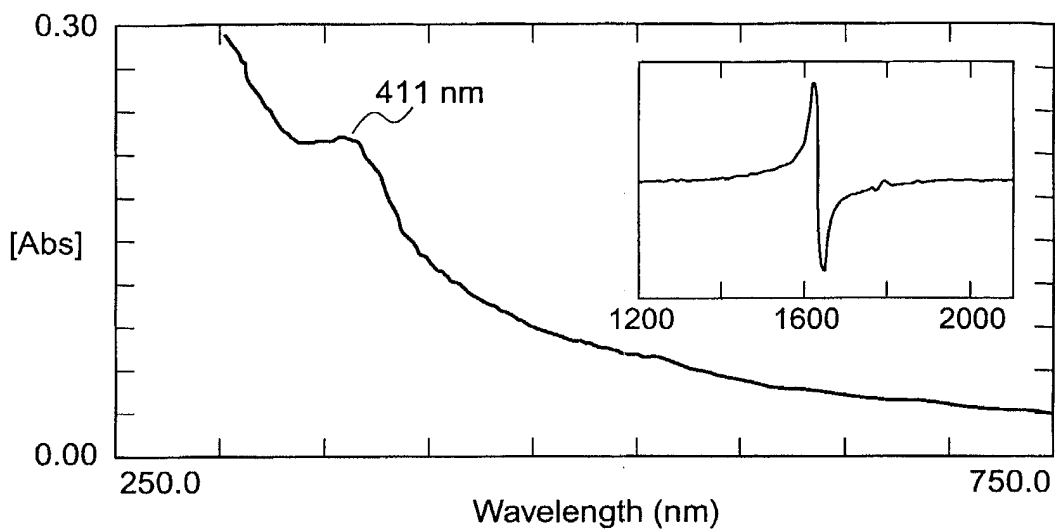


FIG. 4A

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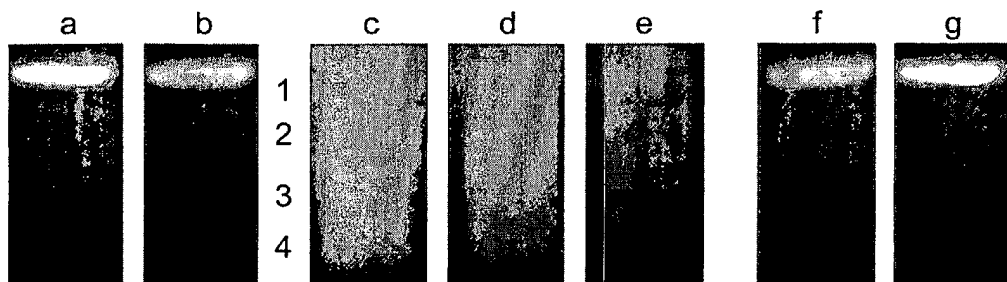


FIG. 4B

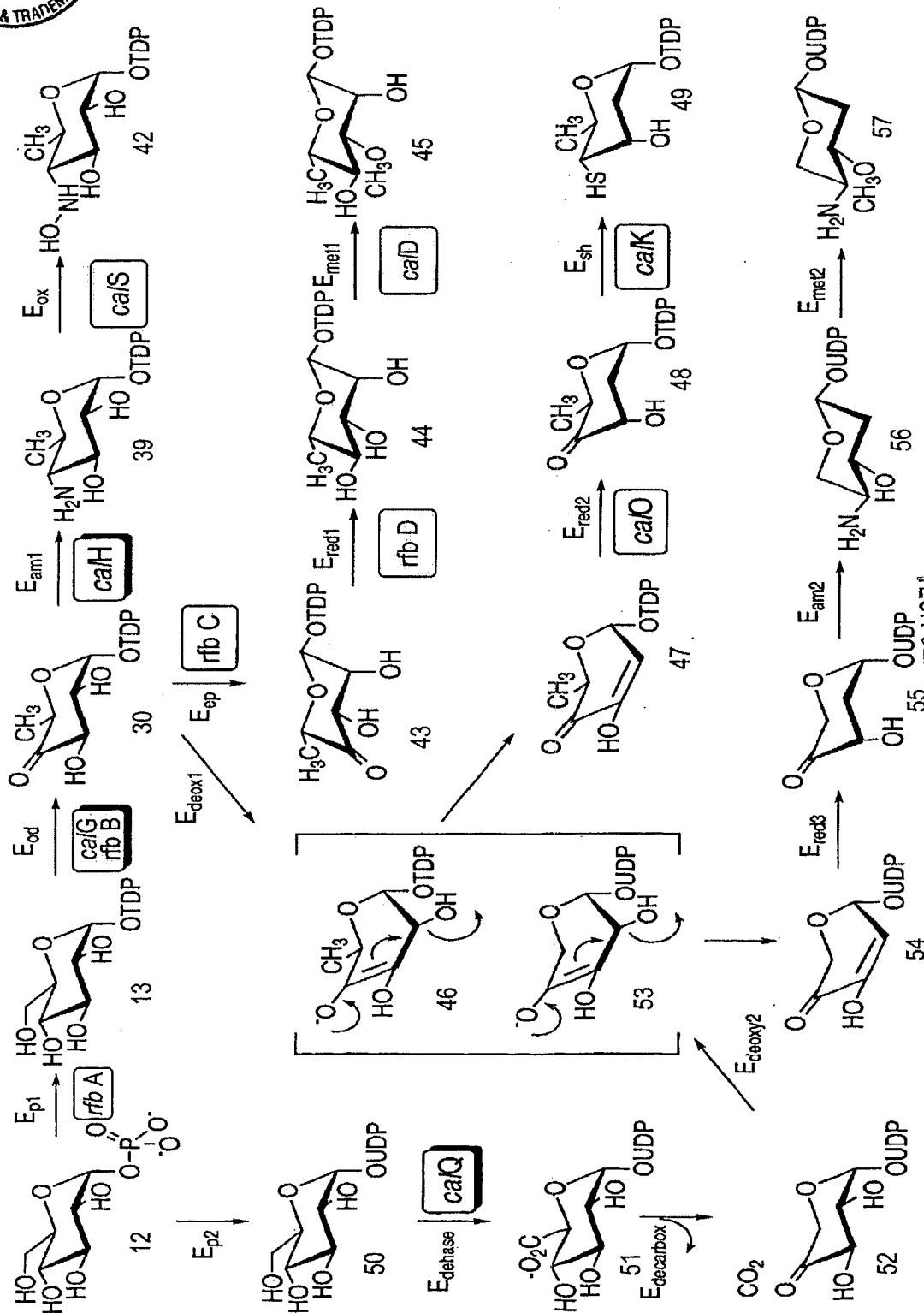


FIG. 5

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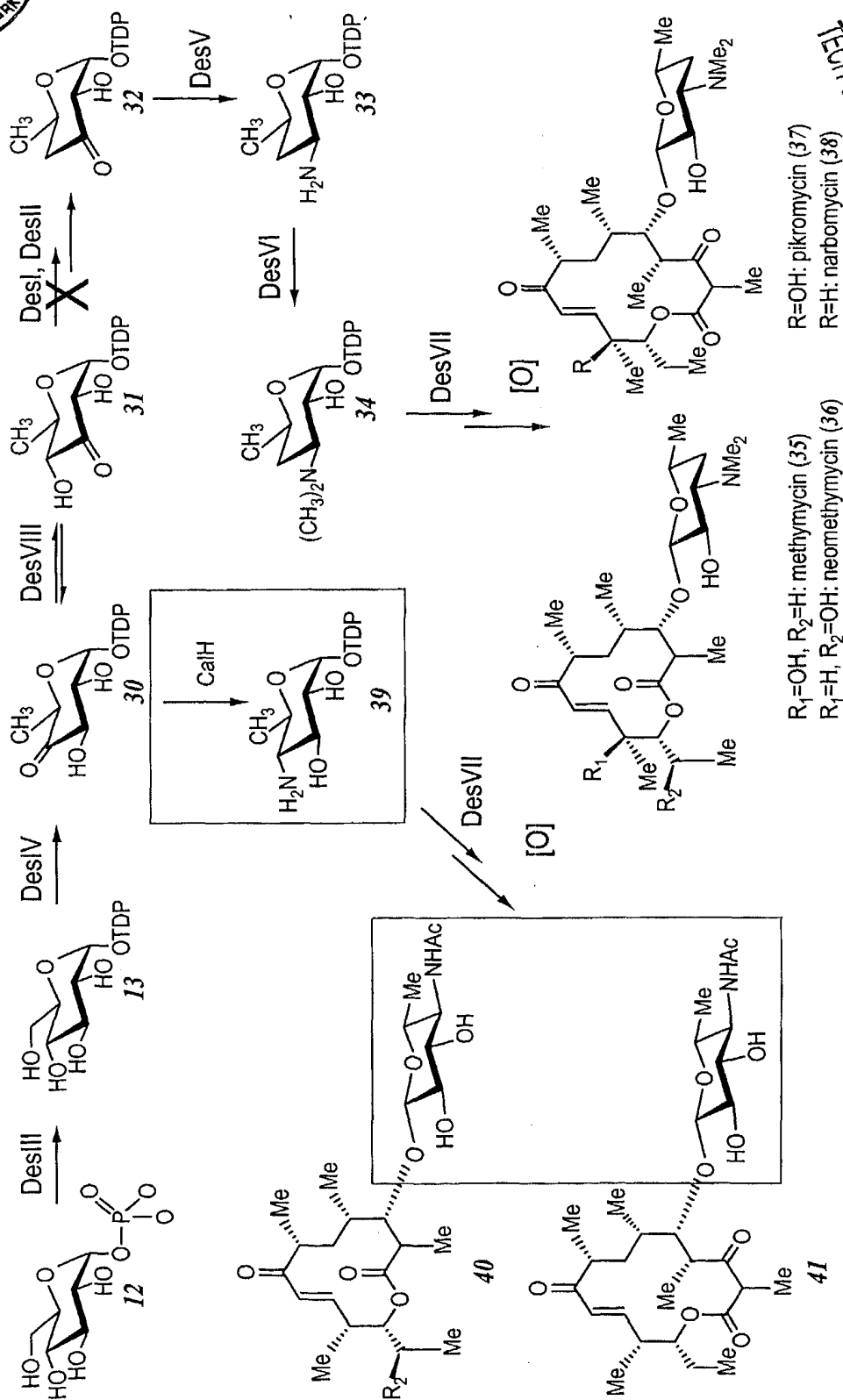


FIG. 6

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Me — NHAC

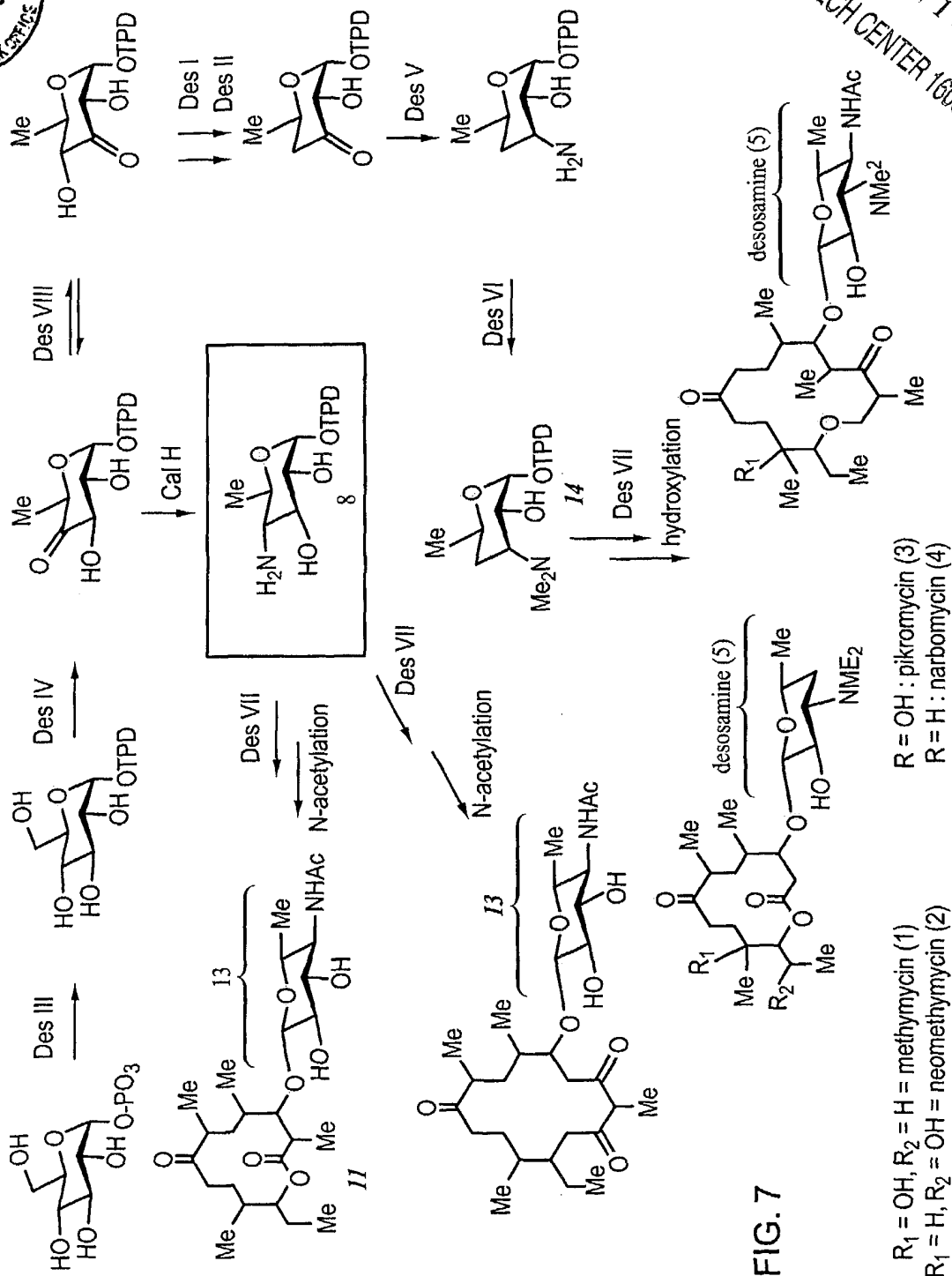


FIG. 7

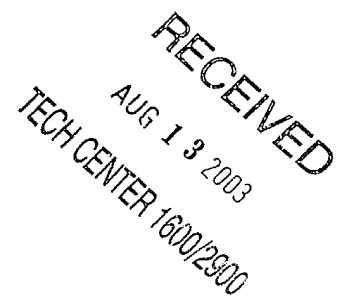


FIG. 8

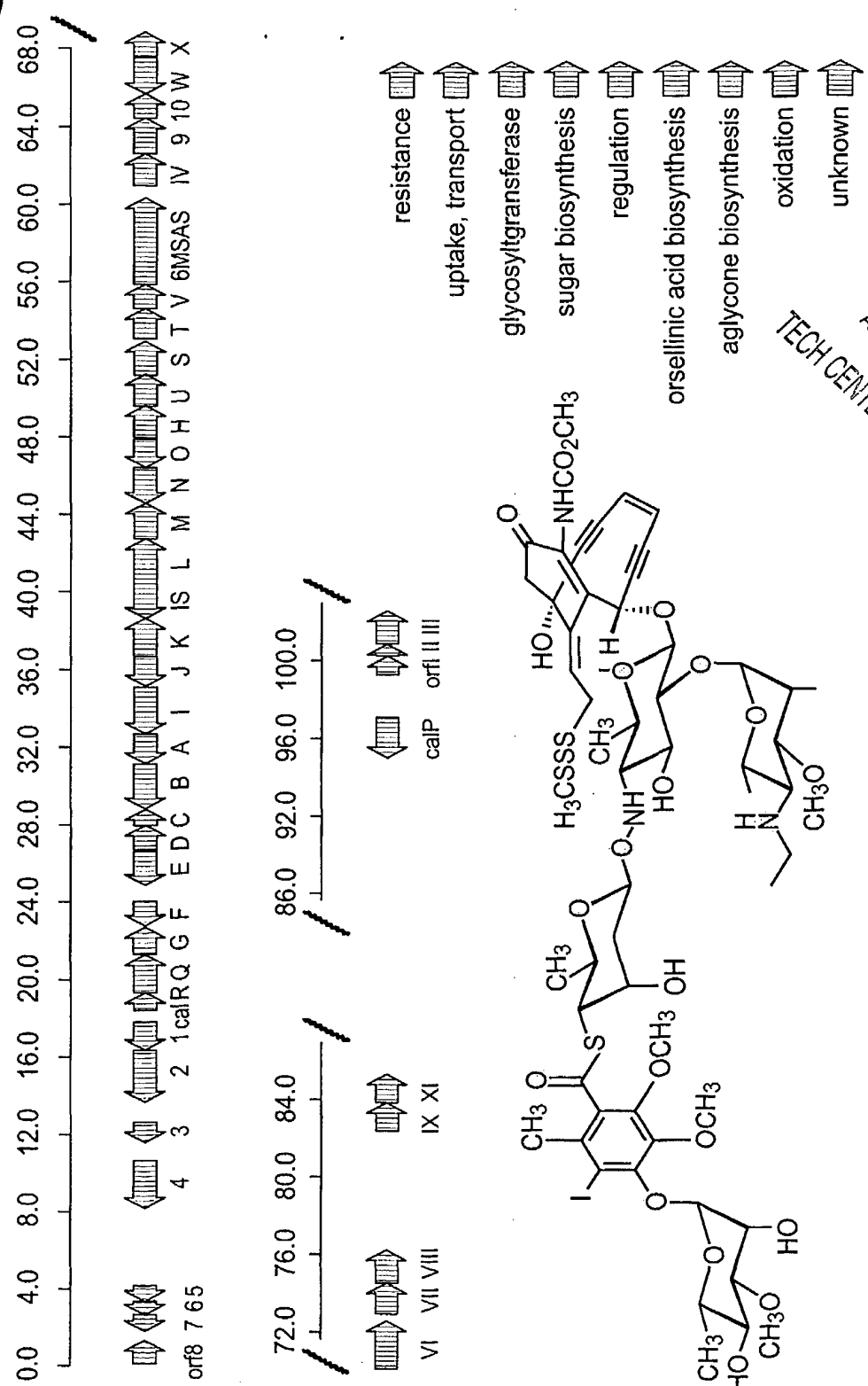
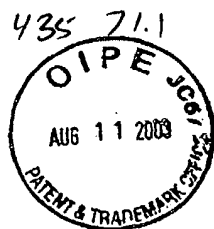


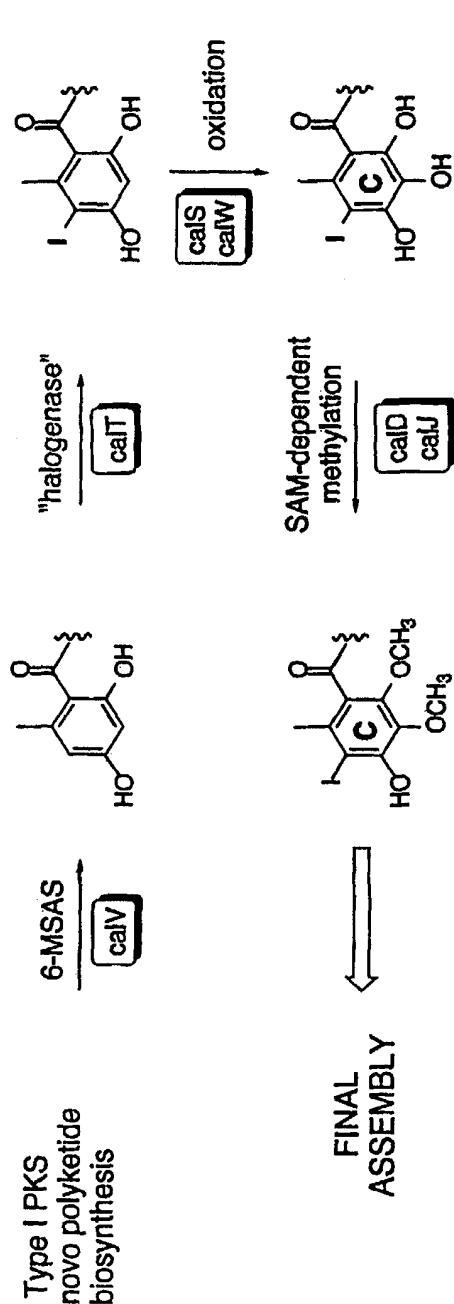
FIG. 9

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The Aryltetracarboxide Unit (a type I PKS product):



Synthesis of Putative Substrates:

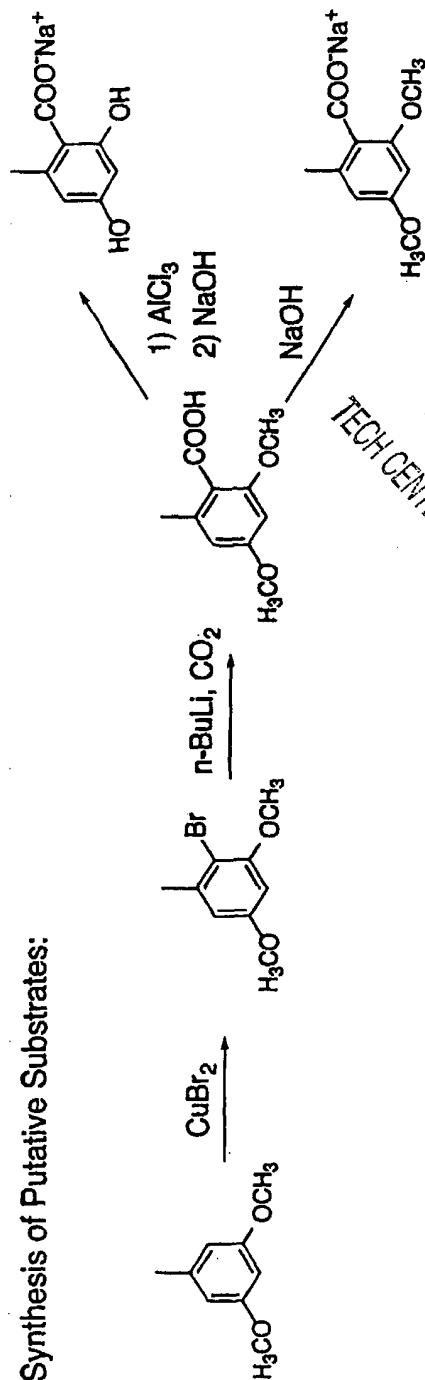


FIG. 11

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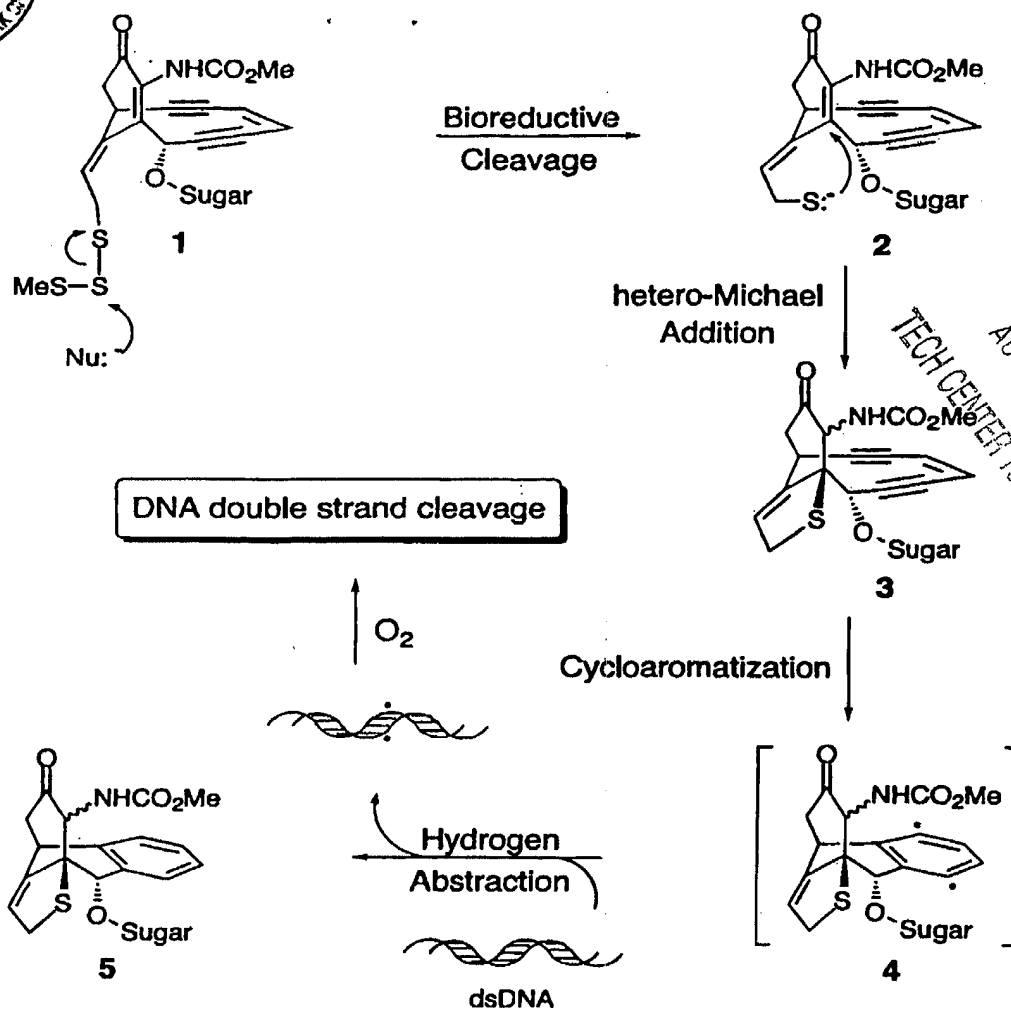


FIG. 12

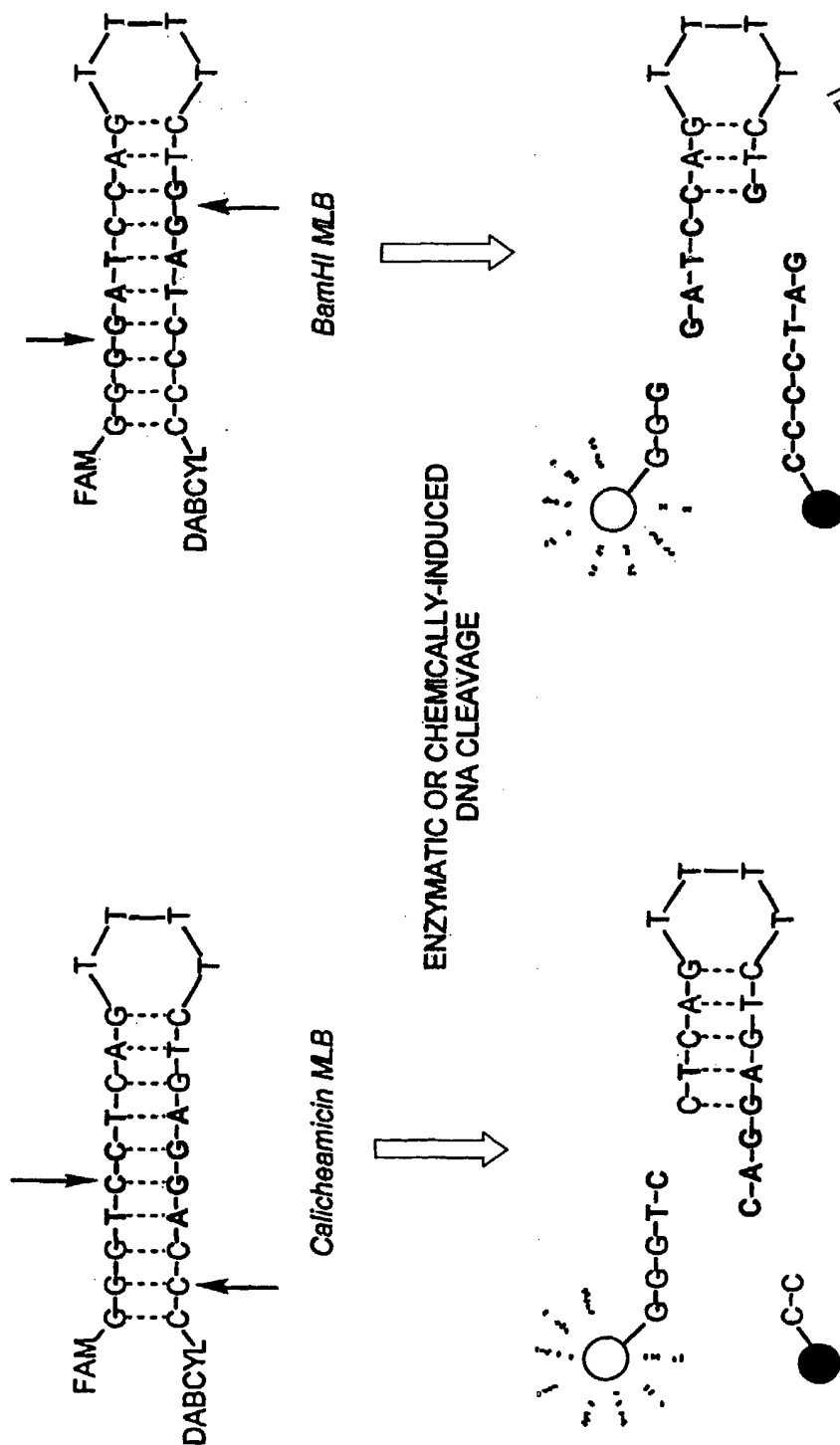
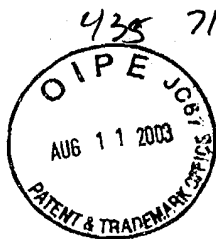


FIG. 13

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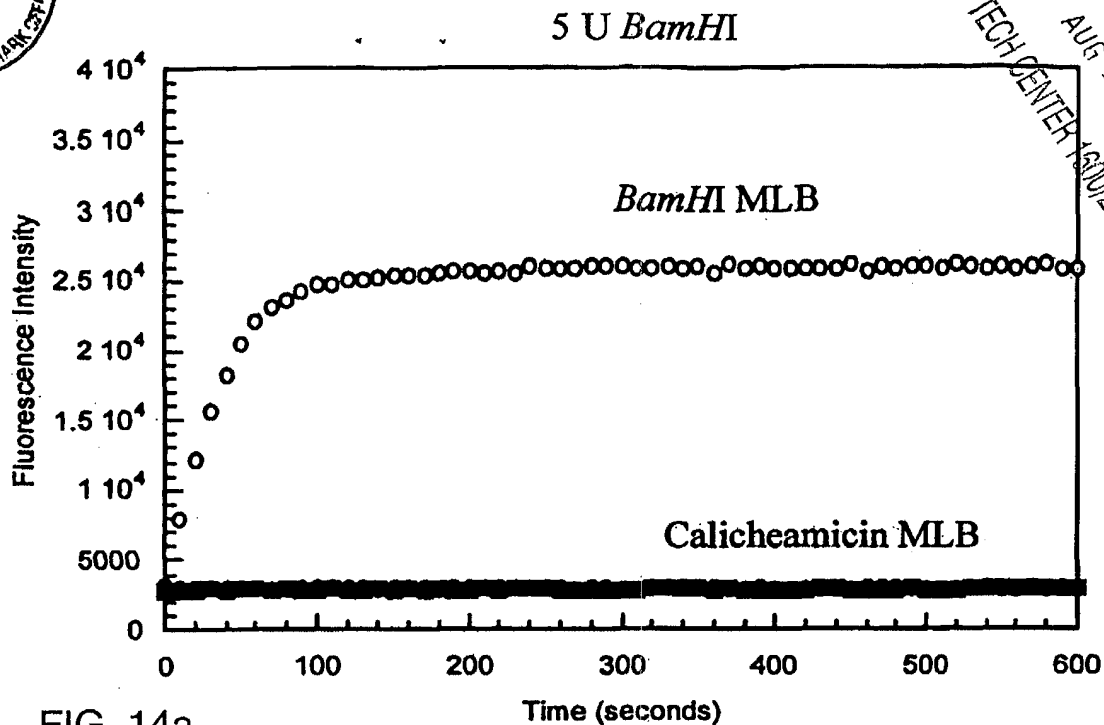


FIG. 14a

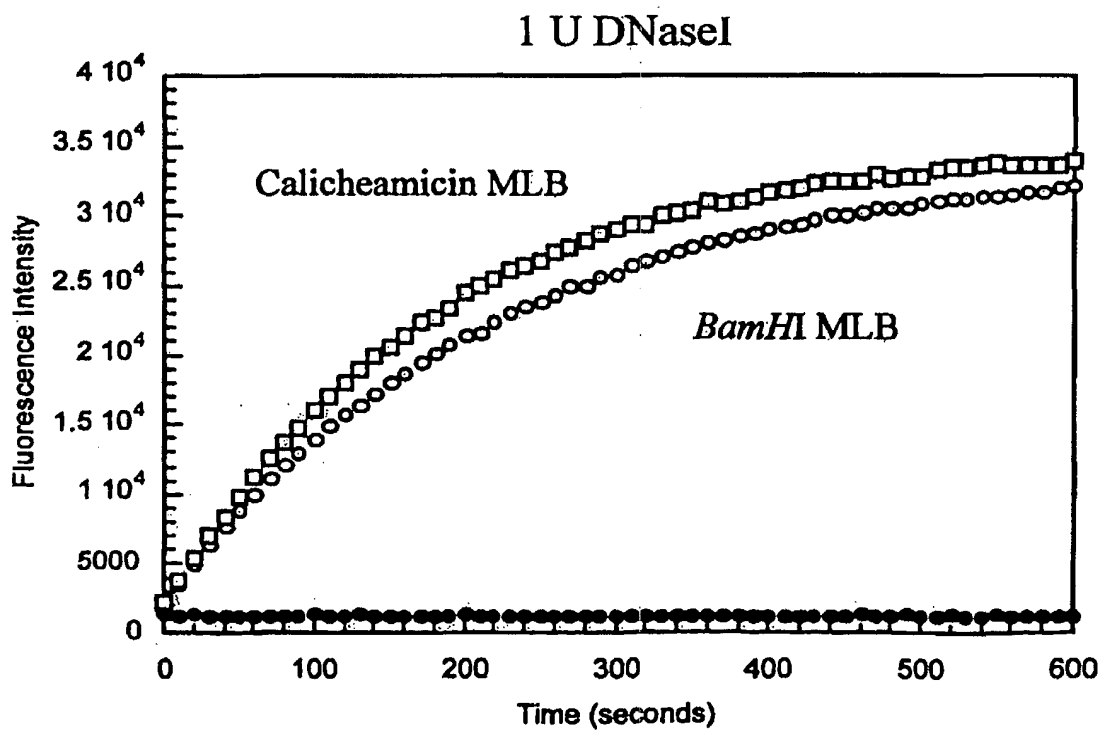


FIG. 14b

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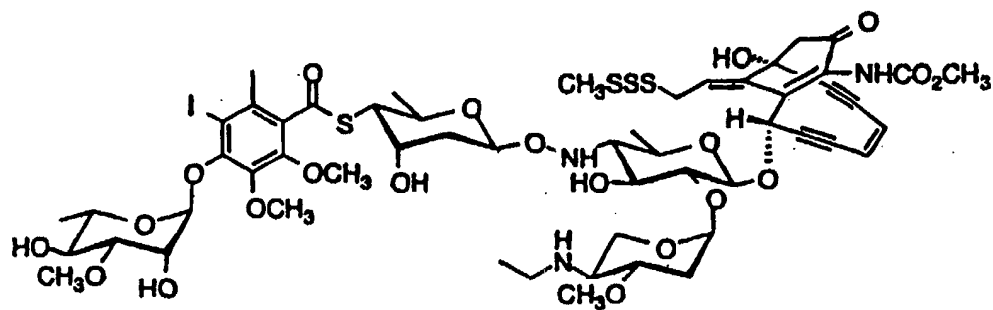
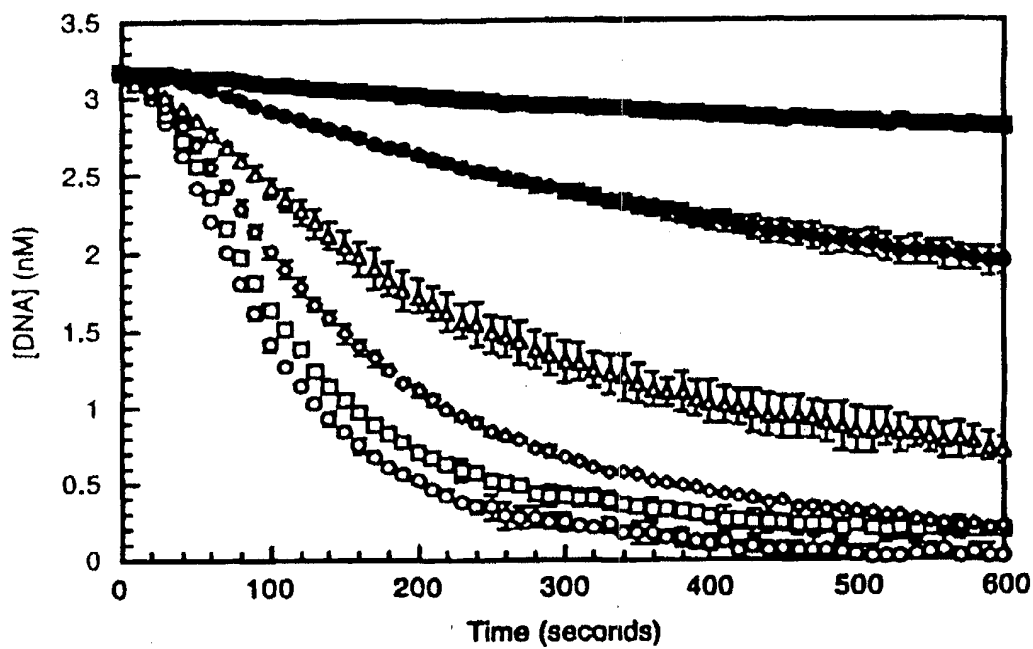
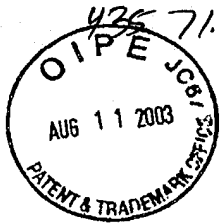


FIG. 15a



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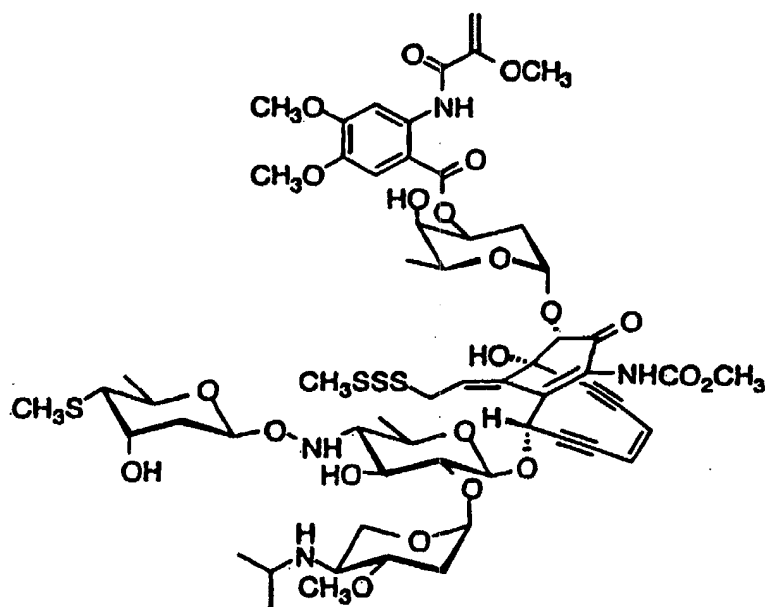
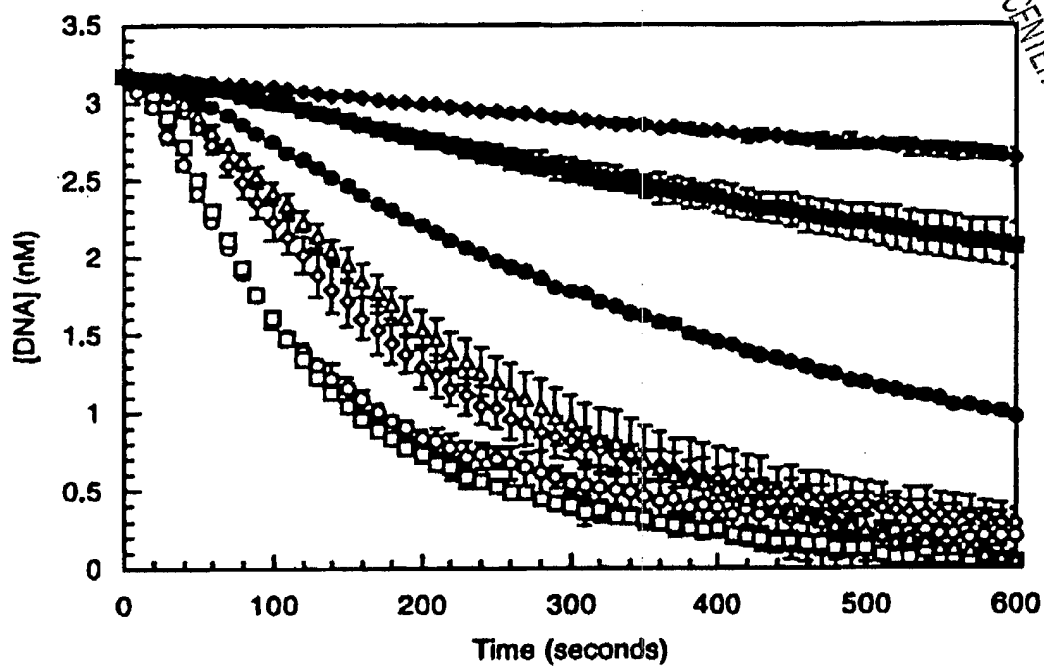
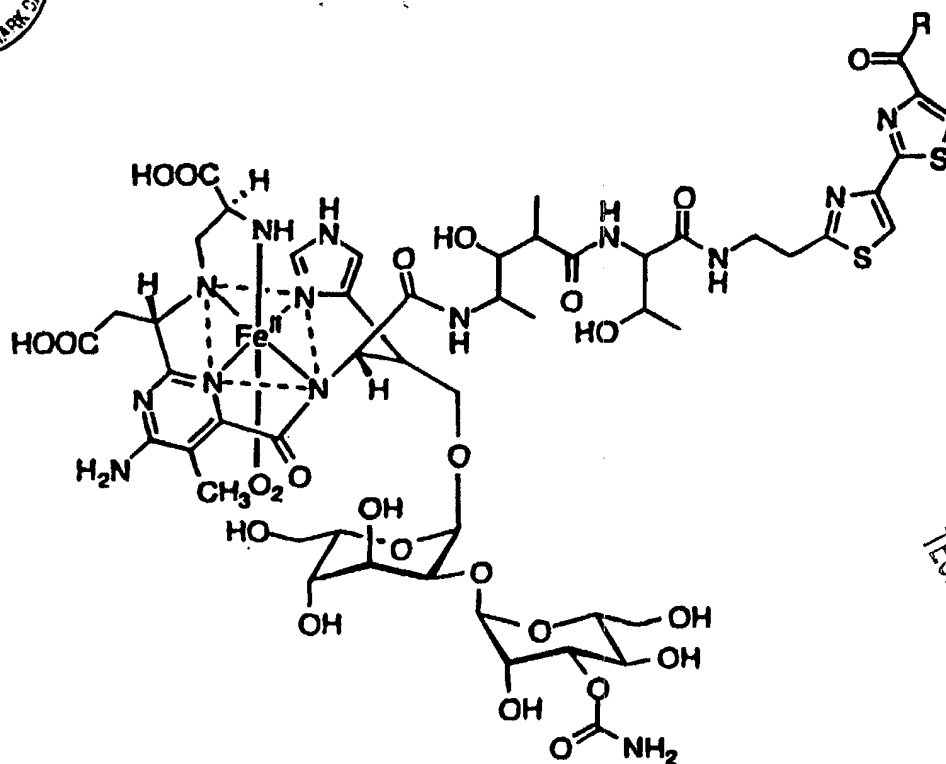


FIG. 15b



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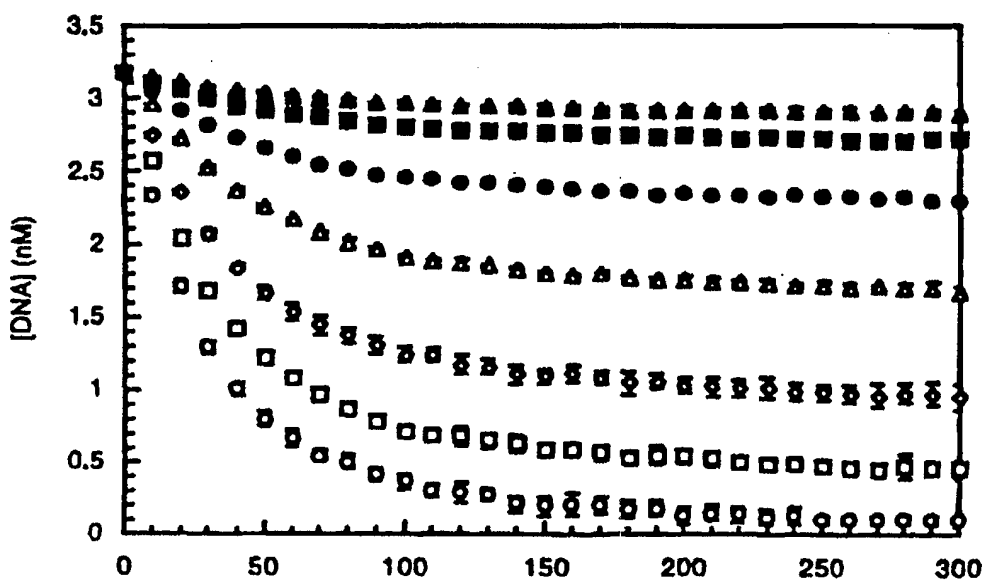
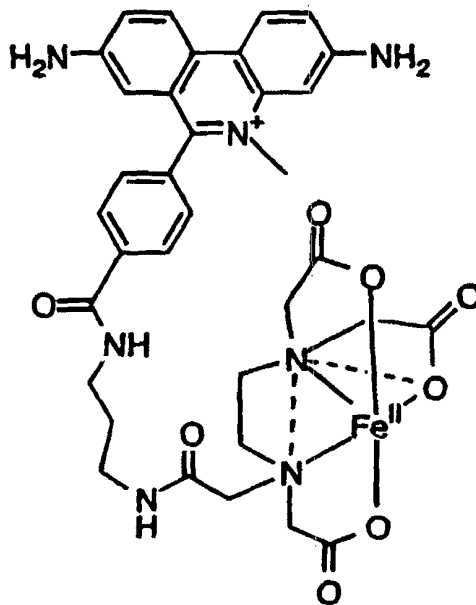
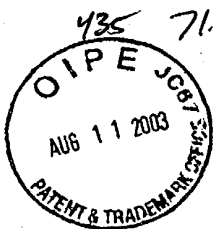


FIG. 16a



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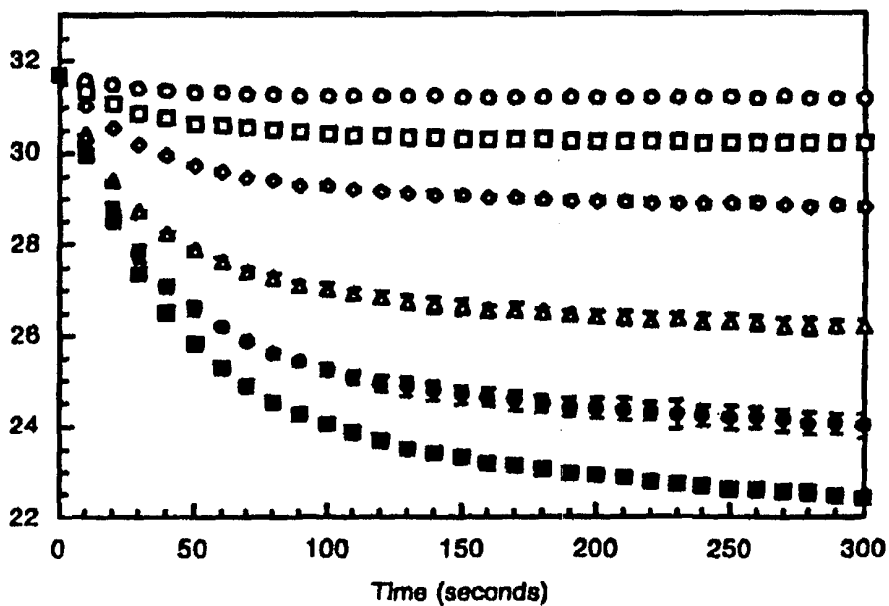
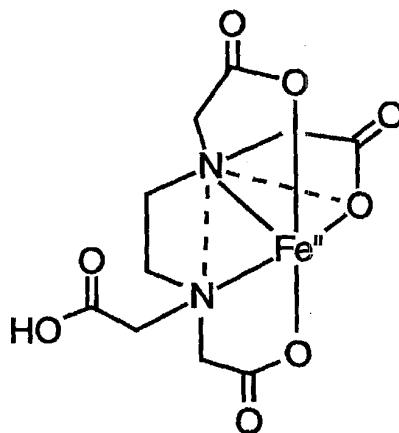


FIG.16c



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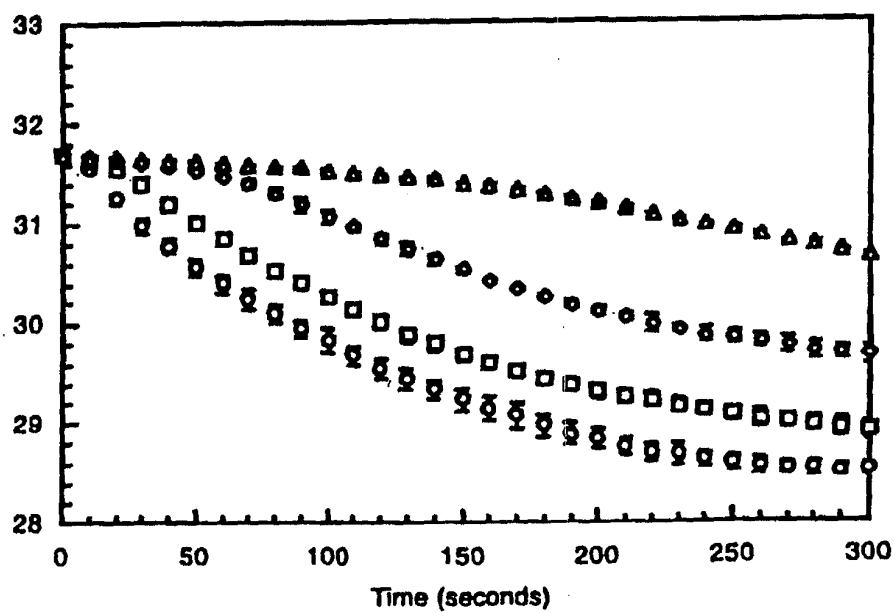


FIG. 16d

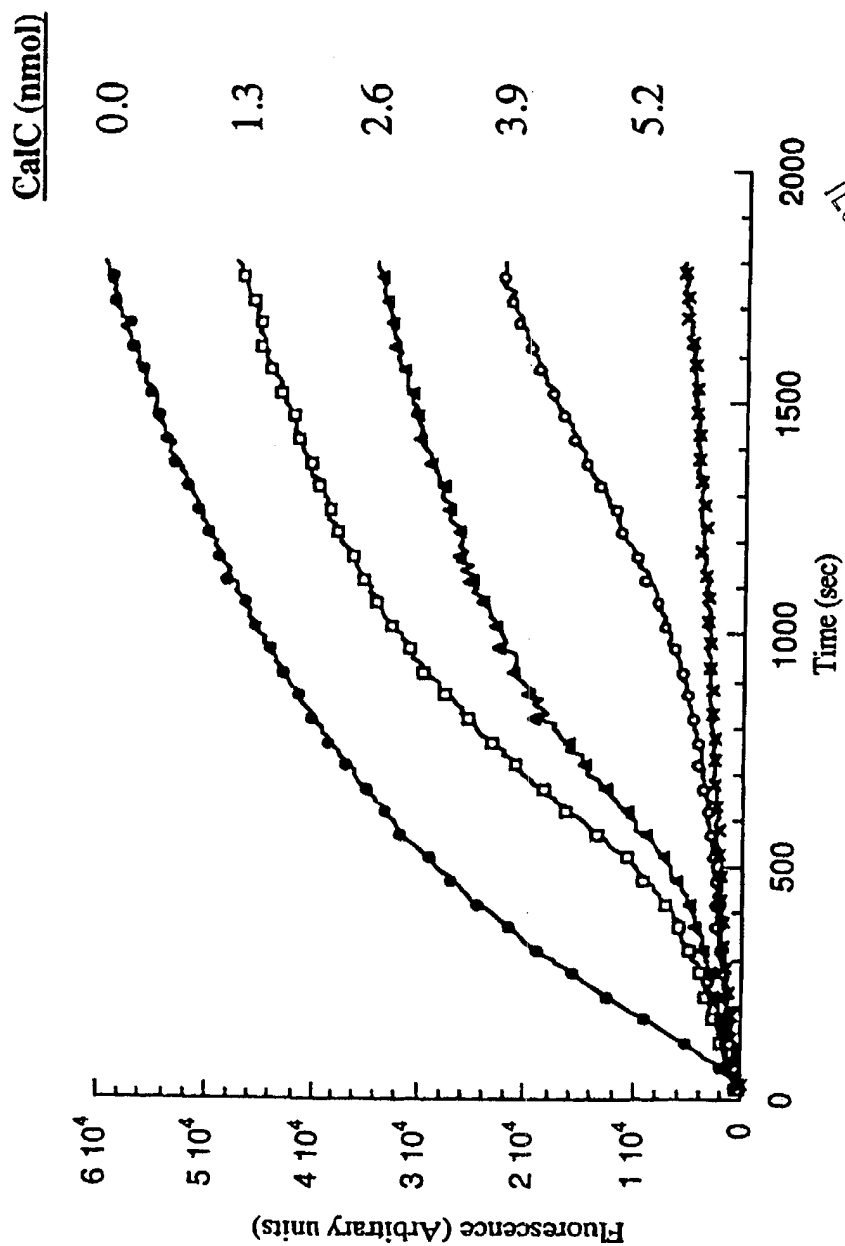


FIG. 17

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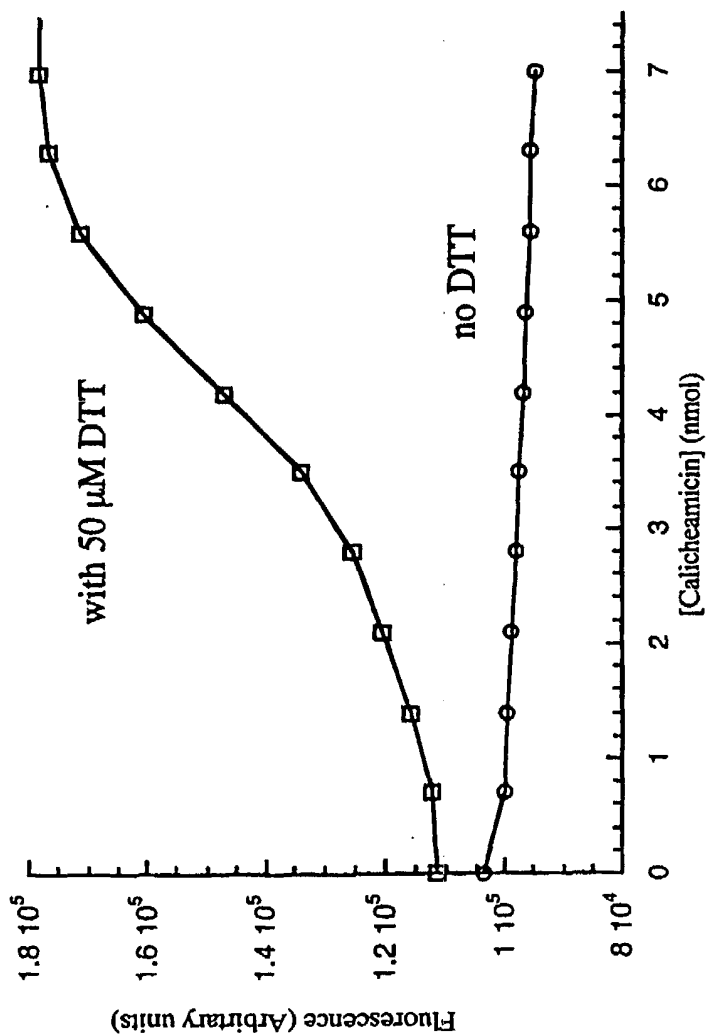
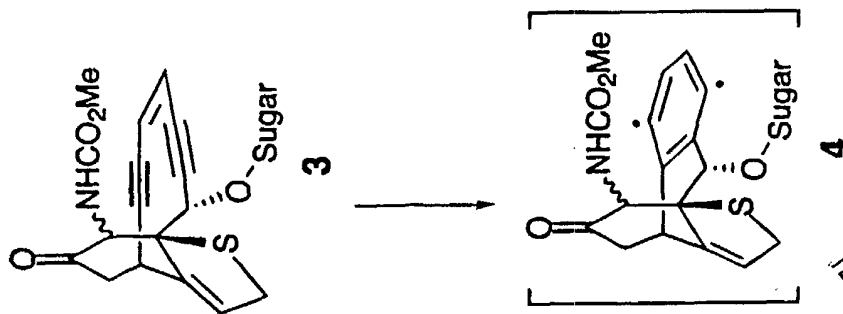
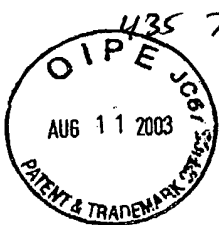


FIG. 18

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